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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,209	04/17/2006	Hideakira Yokoyama	2006-0565A	8796

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EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
12/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,209	YOKOYAMA ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,8 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6,8 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/17/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed September 17, 2008, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Specification

1. The amendment filed September 17, 2008 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the generic terminology added in response to the objection to the specification for the use of the trademark Aspartame® without accompanying generic terminology has not been supported by the filing of an affidavit to support this change. Additionally, the added terminology of "amino acid" is much broader in scope that the trademark Aspartame®, which refers to one specific compound.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1 – 3 and 7 – 9 were rejected under 35 U.S.C. 103(a) as being unpatentable over Nishii et al. (WO 99/55320) and Sequeira et al. (US 5,879,711) further in view of Hart et al. (US 5,422,134). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed June 17, 2008 and those set forth below. Due to the amendments to the claims, this rejection is now applied to claims 1, 2, 6, 8 and 10.

Applicant traverses this rejection on the basis that the jelly formulation of Nishii et al. is not easily gelled by the addition of the organic acid. The gelling can be accelerated by increasing the gelatin concentration, but that increase in gelatin concentration results in a decrease in the ability to release the drug. Neither the stability nor releaseability, only the control of unpleasant taste, is considered by Nishii et al. There is no suggestion which would lead one of ordinary skill in the art to expect that the organic acids used by Nishii et al. and the inorganic acids disclosed by Sequeira et al. would be equivalent. Thus, one of ordinary skill in the art would not have used an inorganic acid in lieu of the organic acid of Nishii et al. Even if such a substitution would have been obvious, that presumption is overcome by the unexpectedly superior results achieved by the present invention when using phosphoric acid in place of the organic acid taught by Nishii et al.

The compositions of Sequeira et al. are directly towards an oral, not topical, treatment and the exemplified gelling agents are distinct from those presently claimed. The pH range disclosed by Nishii et al. is 3.5 to 6 while the instant claims recite a range of 6.0 – 7.4. The water-soluble polymers specified claimed in claim 7, the limitation of which have been incorporated into claim 1, are addressed by the teachings of Hart et al.

The gelling agent compositions of Hart et al. indispensably contain depolymerized locust bean gum, while the water-soluble polymers instantly claimed are polymers and are therefore not depolymerized.

These arguments are not found to be persuasive. In the specification, Applicant has provided one example of the altered drug release of the jelly preparation by the change from citric acid to phosphoric acid. While the two curves in figure are different, no indication is given as to the error associated with these measurements. Also, Nishii et al. uses citric or malic acid and this does not represent a complete comparison between the instant claims and the cited prior art. Beyond this, no other facts regarding the altered stability and/or drug release from the compositions is given. Arguments without factual support are mere allegations and are not found to be persuasive. Therefore, Applicants have not conclusively demonstrated unexpected results for the entire scope of the claims and this line of argument is not found to be fully persuasive. As both organic acids such as citric or malic acid and inorganic acids such as phosphoric can be used to alter the pH of the compositions, they are functionally equivalent and one of ordinary skill in the art would have no reason to expect that switching from an organic to inorganic acid would mean that the pH of the gel solution could not be altered.

The pH range of the instant claims of 6.0 to 7.4 overlaps with the range of 3.5 to 6 taught by Nishii et al. A prima facie case of obviousness exists where there is an overlap in the ranges (see MPEP 2144.05).

It is noted that the features upon which applicant relies (i.e., a topical formulation) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In response to applicant's argument that Sequeira et al is directed towards a topical and not oral composition, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Hart et al. does disclose the use of depolymerized locust bean gum but the gelling compositions also includes a polysaccharide or mixture of polysaccharides which form a gel in combination with the locust bean gum (Col 3, ln 35 – 40). The polysaccharide pectin, which reads on a water-soluble polymer, is exemplified (col 1, ln 30 – 37, 47 – 54) and thus the second ingredient in the gelling compositions of Hart et al. are polymers. The presence of other ingredients such as depolymerized locust bean gum is not excluded due to the use of the open language of comprising in the instant claims.

Newly added claim 10 recites a range for the amount of biguanide drug of 200 to 2250 mg. Nishii et al. discloses dosages of the biguanide metformin are about 250 mg and about 850 mg per dose (p 1, ln 11 – 13).

6. Claims 1, 2, 6, 8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nishii et al., Sequeira et al. and Hart et al. further in view of Sumiya (English translation of JP2000212544).

As discussed above and in the Office Action mailed June 17, 2008, Nishii et al., Sequeira et al. and Hart et al. discloses pH controlled gels, using either organic or inorganic acids, of biguanide drugs such as metformin wherein the gelling agent can be a variety of polymers such as pectin. A pH range of 3. 5 to 6 decreases the unpleasant taste and keeps the active ingredient stable (col 2, ln 34 – 37 of Nishii et al.).

None of the references disclose a pH of greater than 6.

Sumiya discloses stable shape retention polysaccharide gels (¶ [0001]). As the pH of the aqueous gel becomes acidic, the decomposition of the polysaccharides results in a softening and/or water separation from the gel (¶ [0002]). By controlling the pH of the gel to a range of pH 5 or higher (¶ [0006]), such as 6 – 9 and 7 – 9 are more preferable (¶ [0008]), the shape retention of the gel is maintained while the adverse effects on other additives is not exerted (¶ [0009]). As shown in the formulation in ¶[0024], a gel with a pH of 7.2 using a phosphoric acid buffer system and 1.00 wt% mastic gum is obtained.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teachings of Sumiya regarding the pH of aqueous polysaccharides gels into the biguanide jelly containing compositions taught by Nishii et al., Sequeira et al. and Hart et al. The pH of the jelly preparations is a results effective parameter. The amount of a specific ingredient in a composition is clearly a result

effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. Sumiya teaches that too low of a pH can have a negative impact on the stability of the gel preparation, too high a pH can exert negative impact on additives in the gel and Nishii et al. discloses that the pH of the preparation is important for the bitterness and stability of the biguanide active ingredient. One of ordinary skill would optimize the pH to achieve a balance between the stability of the active ingredient and other additives, the bitterness of the composition and the stability of gel preparation itself.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW